

DISSERTATION ON

**“EFFECT OF INTRATYMPANIC
GENTAMICIN THERAPY IN MENIERE’S
DISEASE”**

Submitted in partial fulfillment of the requirements for

M.S. DEGREE BRANCH – IV OTORHINOLARYNGOLOGY

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CERTIFICATE

This is to certify that this dissertation entitled
**“EFFECT OF INTRATYMPANIC GENTAMICIN THERAPY IN
MENIERE’S DISEASE”** Submitted by **Dr SURESH. V**, appearing for M.S.
ENT, Branch IV Degree examination in April 2011 is a bonafide record of work
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INTRODUCTION

Prosper Meniere was the first person to describe the symptoms of Meniere's disease in 1861. He proposed that the pathologic locus was in the labyrinth.

Meniere's disease is a disorder of the inner ear. The symptom complex of Meniere's disease consists of spontaneous, episodic attacks of vertigo, fluctuating sensorineural hearing loss, tinnitus, sensation of aural fullness. Meniere's disease is often idiopathic and it can be caused by distention of endolymphatic space. Incidence of Meniere's disease is more common in patient attending neuro otology clinic with dizziness. This disease has peak incidence in working age group between 30 to 60 years.

Gentamicin is an amino glycoside antibiotic that is preferentially toxic to the dark cell and hair cells of the vestibular labyrinth. It is less cochlea toxic when compared with other amino glycoside.

Now the gentamicin perfusion has emerged as a predominant therapy for incapacitating the vertigo of Meniere's disease.

This study has been done to find out the effect of intratympanic gentamicin therapy in Meniere's disease.

AIMS OF STUDY

- To diagnose the patients with very definite and definite Meniere's disease using electrocochleography.
- To study the effectiveness of intratympanic gentamicin therapy in vertigo control.
- To compare the intratympanic gentamicin therapy and oral therapy in Meniere's disease.
- To study the post intratympanic gentamicin therapy electrocochleographic changes.
- To study the changes in hearing level, pre and post intratympanic gentamicin therapy.

REVIEW OF LITERATURE

ANATOMY OF INNER EAR:

The inner ear (or) labyrinth lies in the petrous part of the temporal bone. The inner ear has two part bony labyrinth and membranous labyrinth. Bony labyrinth consists of vestibule, semicircular canal and bony cochlea. Vestibule is a small ovoid bony chamber situated between the medial wall of the middle ear and lateral end of the internal auditory meatus. On the lateral aspect the fenestra vestibule is closed by the foot plate of stapes. On the medial aspect, it has depression for the saccule, utricle and cochlear duct.

There are three semi circular canals superior, lateral and posterior and they lies in planes at right angle to each other. Each canal has an ampullary end which opens independently in the vestibule. The non ampullary end of the lateral semi circular canal open in independently while that of posterior and superior semi circular canal unit to form a common opening called crus commune.

The angle formed by three semi circular canals is the **solid angle**. The **truatman's'triangle** is bounded by bony labyrinth anteriorly, sigmoid sinus posteriorly and superior petrosal sinus superiorly.

THE STRUCTURE OF THE COCHLEAR DUCT:

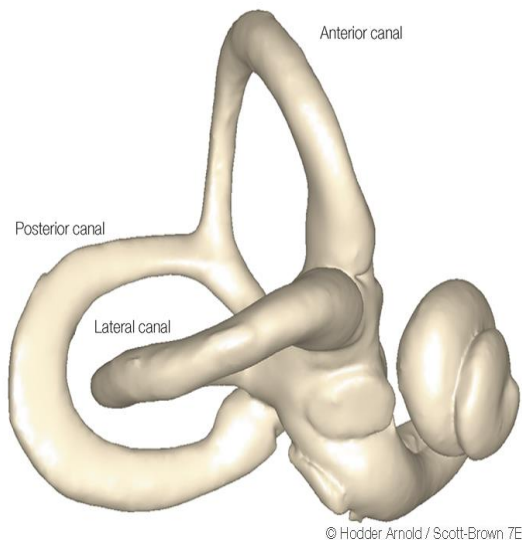
The cochlear duct is subdivided by two longitudinally running membranes that separate three chambers, the scala tympani, scala media, and scala vestibuli. The organ of corti runs in a spiral along the floor of the scala media. The scala media in triangular section has the lower boundary formed by basilar membrane. Upper boundary is represented by the Reissner's membrane. This runs obliquely with respect to the basilar membrane from the spiral limbus near

the modiolus, to the lateral aspect of the bony wall. The basilar membrane stretches across the cochlear duct from a bony shelf spiralling around the central bony modiolus, the osseous spiral lamina to a bony promontory, the spiral prominence.

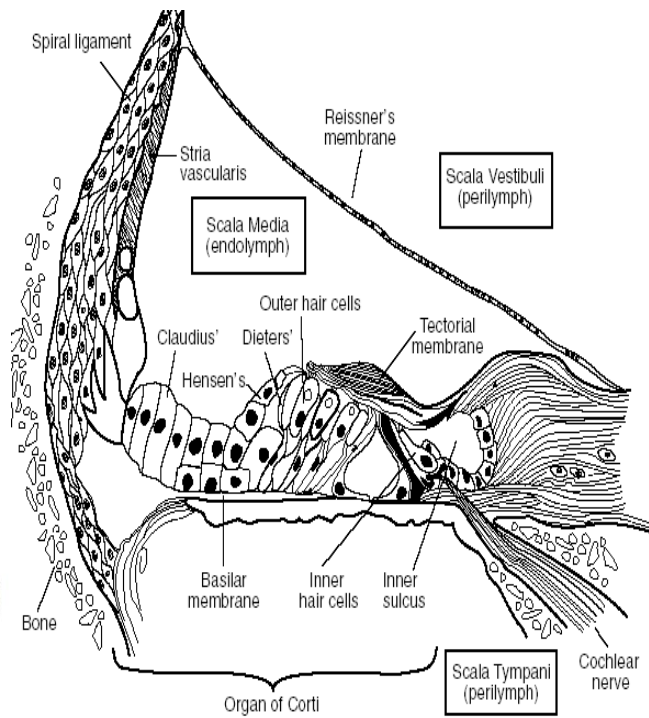
The organ of corti extends across the upper surface of the basilar membrane from the spiral limbus to the Claudius' cells. Underneath the basilar membrane is a layer of spindle shaped cells, the tympanic cells. The branching spiral vessel lies under the basilar membrane.

The longitudinal ridge of the spiral limbus is composed of a layer of interdental cells forming its upper surface and a main body containing blood vessels and connective tissue cells embedded in extracellular matrix. The side of the limbus facing the organ of corti is concave. The concavity is a lined sulcus, which borders the region of the organ of corti, containing the sensory cells and the supporting cells. An acellular flap, the tectorial membrane forms a thin layer over the weakly convex top of the spiral limbus and projects over the inner sulcus and across the organ of corti.

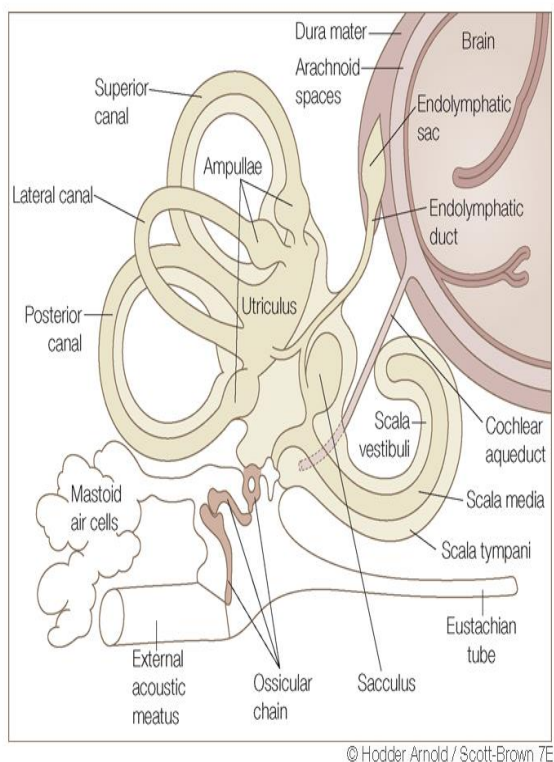
Reissner's membrane consists of two layers of cells separated by a basement membrane. The layer facing into the scala tympani is the mesothelial cell layer. Facing the scala media is the endothelial cell layer.



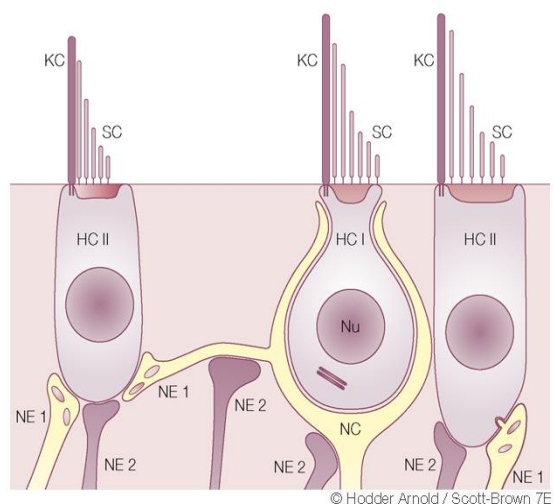
INNER EAR



ORGAN OF CORTI



ENDOLYMPHATIC SAC



COCHLEAR HAIR CELLS

The cells within each layer are joined by tight junctions who act as an impermeable barrier to ions and small molecules

The lateral wall consists of the stria vascularis composed of three layers of cells. There are marginal cells facing the scala media, the intermediate cells and the basal cells. The marginal cells have tight junctions connecting them together.

The cells of the lateral wall contain a variety of ion pumps, enzymes and transport proteins associated with homeostatic mechanisms for maintaining the ionic composition of the fluids of the cochlea ¹⁸.

THE FLUID SPACE OF COCHLEA

The principal division of the fluid space in the cochlea is the perilymphatic space within the scala vestibuli and scala tympani, and the endolymphatic space within the scala media. The walls surrounding the endolymphatic space have occluding tight junction between the cells, obstructing the movement of ions in and out of the cell. The perilymphatic space surrounds the membranous labyrinth and opens into the cerebrospinal fluid by the cochlear aqueduct. The endolymphatic space is joined to the endolymphatic sac by means of the endolymphatic duct.

FORMATION AND ABSORPTION OF THE ENDOLYMPH AND PERILYMPH

ENDOLYMPH

The endolymph of the cochlea is formed by the stria vascularis, which are secreting cell. Under the light microscope, the cells of the stria vascularis can be divided into superficially located darkly staining cells, called the marginal cells, and more lightly staining the basal cells. Under the electron microscope it can

be seen that the marginal cells have long infoldings on their basal edge, across which most of the energy-consuming pumping of the stria vascularis takes place. The stria vascularis has a high concentration of Na^+/K^+ -ATPase, adenyl cyclase, carbonic anhydrase, and oxidative enzymes associated with active pumping of ions and transport of fluid into the endolymph.

The endolymphatic sac contributes to the homeostasis of the endolymph. The cells in the sac are columnar shape and containing long microvilli on the luminal surface, with many pinocytic vesicles and vacuoles. It removes the cellular debris and foreign material from the endolymph. Obliteration of the endolymphatic sac and duct causes endolymphatic hydrops.

PERILYMPH

The site of production of perilymph is controversial. The perilymph is not a simple ultrafiltrate of plasma. The K^+ , glucose, aminoacids and proteins are higher concentration than the CSF. When the cochlear aqueduct is blocked only the concentration of scala tympani is rises, the scala vestibule concentration is the same. It suggests that the perilymph of scala vestibuli primarily originate from the plasma, while the perilymph of scala tympani originates from both csf and plasma.

THE COMPOSITION AND ELECTRICAL POTENTIAL OF THE COCHLEAR FLUID

Endolymph

The endolymph has a high K^+ content and low Na^+ content resembling intracellular fluid. The electrical potential is strongly positive ranging from +50 to +120 mV with respect to plasma. The higher values found in the basal turn and also near the stria vascularies ². The positive endocochlear potential is

directly dependent on $\text{Na}^+\text{K}^+-\text{ATPase}$ in the marginal cells of the stria vascularis ¹⁸.

Perilymph

The values are in the range of normal extracellular concentration, although the K^+ concentration are somewhat higher in scala vestibule than scala tympani. The electrical potential of the scala tympani is +7 mV found to be little positive than that of the scala vestibule +5 mV.

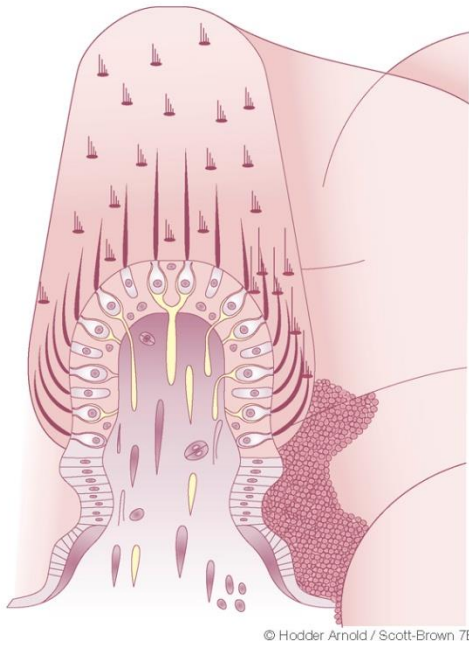
ULTRASTRUCTURE AND FUNCTION OF HAIR CELL

Outer hair cell

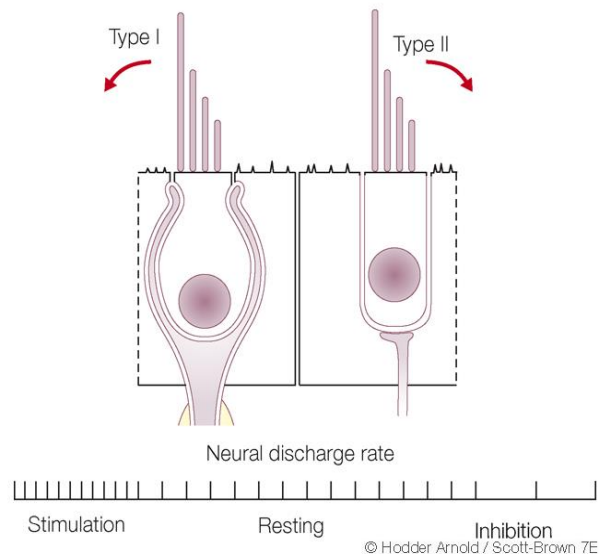
The apical part of the outer hair cell is a sensory end, bearing the stereociliary bundle. The basal end consists of the synaptic pole where the cell connects the afferent and efferent nerve fibers.

The apical surface is flattened, whilst the cell body is cylindrical. The stereocilia are arranged in five rows. The rows increase along the bundle, like a staircase. The outer hair cells in the top of the bundle are in the contact with the tectorial membrane, while inner hair cell is standing free.

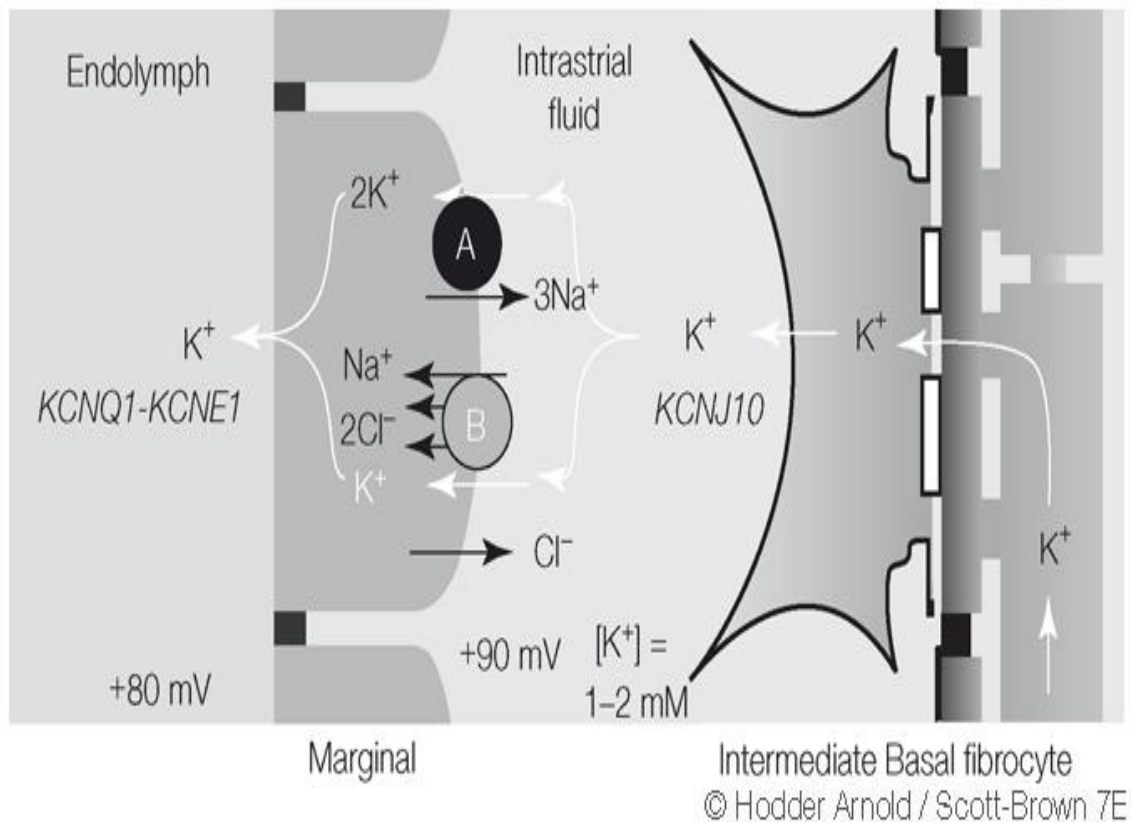
The stereocilia are cylindrical, narrowing sharply having beveled tip in the intermediate rows. The stereocilia contain a core of actin filaments cross linked by actin associated proteins, plastin and espin. The stereociliary membrane contains proteins associated with calcium control (plasma membrane calcium ATPase) and mechanosensitivity (mechanoelectrical transduction channel). There may also be other channels, ATP gating receptor and acid sensing channel.



CRISTA AMPULLARIS



VESTIBULAR HAIR CELLS



During transduction, they are gated mechanically by movements of hair bundle. Deflections of bundle are driven by the motion of basilar membrane-organ of corti complex that causes shearing of the tectorial membrane parallel to the surface of the organ of corti. This in turn directly drives the outer hair cell stereociliary bundle backward and forwards. Deflections in the direction of increasing stereociliary height depolarize the outer hair cell by causing the channels to open and allow influx of cations. Whilst opposing deflections hyperpolarize the hair cell by closing the channel ¹⁹.

Inner hair cell

The inner hair cells have a flattened or slightly concave apical surface, and a flask shaped cell body with a wide center tapering basally and apically. The stereociliary bundle consists of three to four rows. Each rows of stereocilia are similar height. The stereocilia are cylindrical actin- containing structures as in the outer hair cell. The stereocilia are again connected together by filamentous lateral links, which binds both sideways and across the rows. The process of transduction by inner hair cell is similar to that of outer hair cell.

ULTRASTRUTURE OF THE VESTIBULAR ORGAN

The vestibular organ consists of a delicate system of membranous ducts containing sensory epithelia or mechanoreceptors important for the sense of gravity and balance. The sensory epithelium is located in the three ampullae of the semicircular canals and in the macula of the saccule and utricle.

The vestibular organs contain endolymph and are surrounded by perilymph fluid. The membranous system or labyrinth due to its complexity is connected to the cochlea through the thin reunion duct. The various portion of the vestibular organ are interconnected by small canals. The utricular and saccular

duct merge and to form the utriculosaccular duct. This canal runs posteriorly and enters the internal aperture of the bony vestibular aqueduct.

It forms the endolymphatic duct which widens triangularly within the posterior surface of the petrous bone into the endolymphatic sac.

The endolymphatic sac ends blindly within a dural duplicature in the posterior cranial fossa in close association with the sigmoid sinus and venous drainage of the brain. The endolymphatic sac consists of both an intraosseous and an extraosseous portion. The surface of the intraosseous portion of the sac is irregular and tubular, while the surface of the extraosseous portion is usually more smooth and flat.

The endolymphatic sac and duct, which are closely related to the brain, are involved in the reabsorption of endolymph and regulation of perilymph pressure.

Vestibular sensory cells, type I and type II

The type I cells are flask-shaped and surrounded by the terminal end of the afferent fiber of the vestibular nerve. Many of the calyces have collateral extensions that end on type II hair cells. Type II hair cells synapse with these collaterals and also directly with the outer membrane of calyces surrounding type I hair cells. Efferent nerve endings also terminate on the afferent nerve calyce and on type II hair cells.

Type I cells, which are found only in birds and mammals, correspond to the inner hair cells of the organ of Corti. Some of the sensory cells are low threshold mechanoreceptors, showing a high degree of adaptation being presynaptic to the large-diameter myelinated neurons in the vestibular nerve.

These highly adaptive cells are thus considered to be associated with neurons showing an irregular discharge pattern. Type II cells, which are thought to be phylogenetically older, resemble outer hair cells of the organ of Corti. They are cylindrical in shape, but have the same arrangement of stereo- and kinocilia as the type I cells. The upper surface of the hair cell contains approximately 70 stereocilia and one kinocilium arranged with the longest stereocilia positioned adjacent to the kinocilium. The stereocilia in the macula are a few microns long, while in the crista they measure up to over 35 μm . The stereocilia contain actin filaments. All the cilia within a bundle move together as if joined to one another. Labelling for electron microscopy with polycationic ferritin reveals that the membrane surrounding the cilia has a surface coat of negatively charged molecules. The upper surface of the cell contains a thicker region, called the 'cuticular plate' into which the stereocilia extend their rootlets.

SUPPORTING AND 'DARK' CELLS

The sensory cells are surrounded by supporting cells whose function may be partly secretory in nature. They may provide support and insulation for the sensory cells and may also form precursor cells for sensory hair cells.

The membranous labyrinth contains so-called 'dark' cells in all sensory epithelia, except the saccule. The cells have an irregular surface and resemble the marginal cells of the stria vascularis. In addition melanocytes are often associated with the dark cells, which is similar to the situation in the stria vascularis of the cochlea¹. These cells are important for the development and maintenance of the unique chemical composition of the endolymph thereby playing a role for the proper function of the electric activity of the sensory cells and initiating conductive neural responses of afferent nerves.

SACCULE AND UTRICLE

The utricle is oblong, irregular and slopes anteriorly upwards at an angle of approximately 30° . It lies superior to the saccule. The macula utriculi are the largest and lie mostly in the horizontal plane located in the dilated superior portion of the utricle. The macula utriculi contain approximately 33,000 hair cells. The saccular macula contains approximately 18,000 hair cells. Overlying the neuroepithelium is a calcareous material consisting of a multitude of small cylindrical and hexagonally shaped bodies with pointed ends, usually named otoconia. These otoconia are anchored and partially embedded in a gelatinous substance forming the otoconial membrane.

The hair process project in to the otoconial membrane and are displaced mechanically by the otoconial mass relative to the sensory epithelium.

FUNCTION OF THE AMPULLA AND CUPULA

The afferents in the horizontal canal are stimulated, when endolymph flows against the utricle. The two vertical canals are stimulated, when endolymph flows against the ampulla. The sensory epithelium on the crista is covered by gelatinous mass called the cupula. The cupula in the ampulla of the semicircular canal helps in transferring endolymph fluid movement stimuli to the hair cells. This gives rise to kinetic reflexes.

MENIERE'S DISEASE

This is common disorder of the inner ear and is sometimes also referred to by its etiopathological nomenclature endolymphatic hydrops. However, the two terms are not synonymous.

DEFINITION

Meniere's disease is a disorder characterized by spontaneous attack of vertigo, with associated fluctuating sensorineural hearing loss, tinnitus, and aural fullness.

ETIOPATHOGENESIS

Endolymph may be either excessively or inadequately resorbed resulting in expansion of the endolymphatic space. Endolymphatic hydrops typically involves the pars inferior of the labyrinth (comprising the saccule and cochlea). Saccular hydrops may range from mild to severe, based on the degree of membrane distention toward the stapes footplate. Cochlear hydrop is bowing of the Reissner membrane into the scala vestibule. Severity of cochlear hydrops also varies according to the degree of convexity toward the scalar wall of modiolus.

The degree of distention appears to be related to the mechanical compliance of membranous components of the inner ear, with high compliance (mechanically weaker membranes) in the scala, lower compliance (mechanically stronger membranes) in the semicircular canal ¹³.

The distention of the endolymphatic duct causes rupture of the membranes, this has been observed throughout the labyrinth. Membrane rupture allows the potassium rich endolymph to leak into the perilymphatic space and contact the basal surface of the hair cells as well as the eighth cranial nerve.

Initial excitation then subsequent inhibition of the hair cells manifest as a direction changing nystagmus and episodic vertigo ¹².

Long term declines in auditory and vestibular function may be the result of repeated exposure of the vestibular hair cells to toxic levels of potassium enriched perilymph. The sparse nerve endings on the basal surface of type II hair cells provide decreased protection against harmful ionic changes in the perilymph ¹³.

Alternatively, the hydrops itself may occur in an episodic manner, as a result of sudden increase in the secretory function of the stria vascularis or the spontaneous obstruction of the endolymphatic sac. Hydropic distention may then cause a mechanical deflection of the macula and crista of the otoliths and semicircular canals, respectively, and thus vestibular hair cells depolarization leading to the sensation of vertigo ¹⁵. Long term changes to the neuro sensory function of the vestibular apparatus may be the consequence of increased hydrodynamic pressure, causing increased vascular resistance, compromised blood flow, and chronic ischemic injury.

SYMPTOMS

1. Vertigo : Vertigo occurs in spells that lasts from 20 minutes to 24 hours, and is usually accompanied by nausea and vomiting. In between two attacks, the patient does not have any significant vertiginous problems.

2. Deafness : Initially low frequency sounds is lost and gradually increases in intensity middle and high frequency sounds. The deafness is usually more marked during the attacks (fluctuating in nature) and Sensorineural type.

3. Tinnitus : A subjective tinnitus is present in most patients during the attacks of vertigo. It is perceptible in the intervening period also.

4. Aural Fullness: The sensation of fullness of the ear usually starts immediately prior to the vertiginous attacks. But the ear fullness subsides after the attack and is usually absent in the intervening period ¹⁷.

AAO-HNS CLASSIFICATION

VERY DEFINITE MERIERE’S DISEASE

- The patient has had at least two attacks of sudden vertigo has lasted more than 20 minutes but less than a day along with Deafness, Tinnitus, Aural fullness, Glycerol dehydration test positive , EcochG positive

DEFINITE MENIERE’S DISEASE;

- Episodic vertigo, Deafness, Tinnitus, Aural fullness, Positive glycerol positive test, Typical EcochG finding not present

PROBABLE MENIERE’S DISEASE;

- Only one episode of severe vertigo of less than 24hrs ,but more than 20mts along with Tinnitus, Aural fullness, Audiometric evidence of hearing loss

POSSIBLE MENIERE’S DISEASE

- Episodic vertigo of the Meniere type without hearing loss, or sensoineural hearing loss, fluctuating or fixed, with disequilibrium but without definitive episodes.

AAO-HNS CRITERIA FOR MENIERE'S DISEASE

Vertigo

- a. Any treatment should be evaluated no sooner than 24 months.
- b. Formula to obtain numeric value for vertigo; average number of definitive spells/ months in a 24 month after therapy $\times 100 =$ numeric value.
- c. Numeric value scale

Numeric value scale	control level	class
0	complete control of definitive spells	A
41-80	limited control of definitive spells	B
81-120	insignificant control of definitive spells	C
>120		D
Secondary treatment initiated		E

Disability

- a) No disability
- b) Mild disability- intermittent or continuous dizziness/ unsteadiness that precludes working in a hazardous environment.
- c) Moderate disability- intermittent or continuous dizziness/ unsteadiness that result in a sedentary occupation.
- d) Severe disability- symptoms so severe as to exclude gainful employment.

Hearing

Hearing is measured by a four frequency pure tone average (PTA) 500Hz, 1 KHz, 2 KHz, and 3 KHz.

Pretreatment hearing level: worst hearing level 6 months prior to surgery.

Post treatment hearing level: poorest hearing level measured 18-24 months after institution of therapy.

Hearing classification:

- Unchanged=10d B PTA ,15% SD
- Improved >10 d B PTA >15% SD
- Worse >10 d B PTA worsened >15% SD worsened.

Hearing level

Stage	Four tone averages (d B)
1	>25
2	26-40
3	41-70
4	>70

Functional level scale

This is subjective scale determined by patient

1. My dizziness has no effect on my activities at all.

2. When I am dizzy, I have to stop for a while, but it soon passes and I can resume my activities. I continue to work, drive, and engage in any activity I choose without restriction. I have not changed any plans or activities to accommodate my dizziness.
3. When I am dizzy I have stop what I am doing for a while, but it does passes and I can resume my activities. I continue to work, drive, and engage in most activities I choose, but I have had to change some plans and make some allowance for my dizziness.
4. I am able to work, drive, travel, and take care of a family or engage in most activities, but I must exert a great deal of effort to do. So, I must constantly make adjustments in my activities and budget my energies. I am barely making it.
5. I am unable to work, drive, or take care of a family. I am unable to do most of the active things that I used to do. Even essential activities must be limited. I am disabled.
6. I have been disabled 1 year or longer and/or I compensation because of my dizziness or balance problem.

AAO-HNS STAGING FOR MENIERE'S DISEASE

STAGE I: PTA 0-25dB, the tinnitus may or may not be perceptible, sense of fullness, vertigo once or twice a year.

STAGE II: PTA 25- 35dB, the tinnitus is mild and perceptible only during concentration, the sense of aural fullness, attack of vertigo 3-4 per year.

STAGE III: PTA 36-50dB, the tinnitus more frequent, aural fullness, attack of vertigo 6-15 per year.

STAGE IV: PTA 50-65dB, the tinnitus is constantly present; sense of aural fullness is persistent, vertigo 3-4 per week.

STAGE V: PTA 66-75dB, the tinnitus is constant, sense of aural fullness is persistent and attack of vertigo is very frequent.

STAGE VI: more than 75dB tinnitus and vertigo incapacitating, sense of aural fullness is persistent.

AUDIOVESTIBULAR TESTING IN PATIENTS WITH MENIERE'S DISEASE

AUDIOMETRIC TESTING

Hearing loss is predominantly sensorineural, fluctuating and progressive. The hearing loss tends to involve the low frequencies early in the course of the disease. Higher frequencies may also be affected, and some have observed a peak, or inverted-V, audiogram in patients with MD. The hearing loss tends to flatten and become less variable. There is no audiometric configuration that can be considered characteristic of MD. Fluctuation of pure tone thresholds, word recognition, or both is commonly noted. In patients with long-standing MD (>10 years), the average pure tone threshold in the affected ear stabilizes at about 50 dB, and the mean word recognition score reaches a minimum of 50%. Profound hearing loss occurs in only 1% to 2% of patients. The sensorineural hearing loss is cochlear in etiology, with associated distortion, loudness recruitment, and a reduction of word recognition scores in proportion to the pure tone average.

LOUDNESS RECRUITMENT

The most straightforward test of loudness recruitment is the alternate binaural loudness balance test (ABLB). Recruitment will show evidence of cochlear pathology.

SHORT INCREMENT SENSITIVITY INDEX (SISI)

SISI test is used to differentiate a cochlear from retrocochlear lesion. In this test, a continuous tone is presented 20 dB above the threshold and sustained for about 2 minutes. Every 5 seconds, the tone is increased by 1 dB and 20 such blips are presented. Patient indicates the blips heard. In conductive deafness,

SISI score is more than 15%; it is 70%-100% in cochlear deafness; and 1-10% in nerve deafness.

TONE DECAY TEST

It is used to detect retrocochlear lesions. Normally, a person can hear a tone continuously for 60 seconds. In nerve fatigue, he stops hearing earlier. A decay more than 25 dB is diagnostic of a retrocochlear lesion.

VESTIBULAR TESTING

Vestibular test results are not included in the 1995 AAO-HNS Guidelines for the Diagnosis and Evaluation of Therapy in MD, and, strictly speaking, are not necessary for the diagnosis of MD.

CALORIC TESTING

Caloric testing represents a non physiologic, low-frequency stimulation of the horizontal semicircular canal. It is the only test in the standard vestibular test battery that provides lateralizing information. This common vestibular test abnormality is reported in up to 50% to 66% of MD patients. This leaves a significant proportion of patients with MD who will have no evidence of pathology on caloric testing. Complete loss of vestibular function as manifested by absent caloric response to ice water irrigation need not be pursued as a therapeutic end point in intratympanic gentamicin therapy, as it is not required for vertigo control in MD.

VESTIBULAR EVOKED MYOGENIC POTENTIALS

Vestibular evoked myogenic potential (VEMP) testing is a more recent addition to the MD diagnostic armamentarium. The VEMP is obtained by measuring the relaxation of the sternocleidomastoid muscle (SCM) in response to an ipsilateral auditory stimulus. Brief high-intensity monaural clicks or tone-bursts produce a

large, short-latency inhibitory potential (VEMP) in the tonically contracted ipsilateral SCM. Although the exact neural pathway is still not fully clear, the VEMP is considered to be a vestibulocollic reflex with the afferent limb arising from sound-responsive sensory cells in the saccule. The afferent signal is conducted centrally via the inferior vestibular nerve, and efferent signal is conducted via the vestibulospinal track to produce inhibitory post-synaptic potentials in cervical motor neurons. Normal responses are composed of biphasic (positive-negative) waves.

VEMP testing is a useful to reveal saccule dysfunction. After the cochlea, the saccule is the second most common site of hydrop changes in temporal bones of patients with MD.

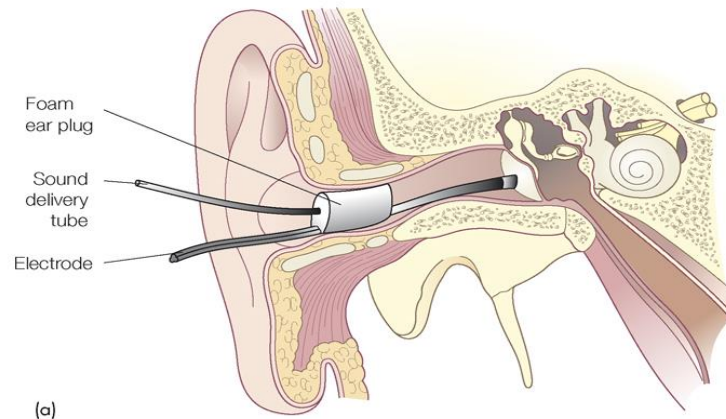
ELECTROCOCHLEOGRAPHY

The cochlea receives the sound from the middle ear and converts it into electrical energy which then passes through the auditory nerve to the higher center in the brain. The electrical activity generated by the cochlea and in the auditory nerve can be measured by a system called electrocochleography. The parameters measured by ECoChG are cochlear microphonic (CM), the summing potential (SP) and the auditory nerve compound action potential (AP). The cochlea microphonic is the electrical activity occurring in the cochlea in response to the sound stimulus, the compound action potential is the electrical activity obtained in the auditory nerve. The summing potential is a complex measurement of many electrophysiological parameters taken together.

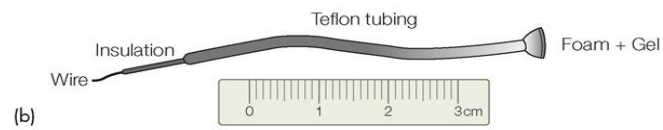
The technique is similar to ABR measurement, in that an auditory stimulus is presented to the test ear and an electrical response is recorded. In the case of ABR, the recording electrode is placed on the scalp, and the response of the auditory nerve and brainstem is measured. The pertinent time epoch consists

of the first 10 ms after stimulus presentation. In the case of EcochG, the recording electrode is placed as close to the cochlea as possible (near-field recording), and the response is measured from the cochlear hair cells and auditory nerve. The epoch of interest is generally within the first 3 ms following stimulus presentation.

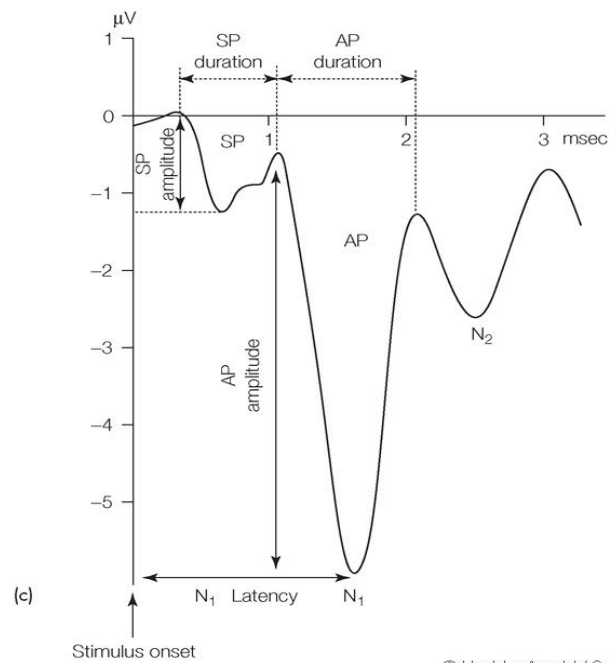
Optimally, the measurement of these potentials is performed with an electrode placed as close as possible to their source to maximize response amplitude. Such near-field recording can be performed with a silver ball electrode placed on the round window membrane. Because this requires surgical exposure of the middle ear, it is not widely accepted for routine outpatient clinical applications. An alternative method is the use of a transtympanic promontory needle electrode referenced to an electrode external to the ear (forehead or tragus). Less invasive recording may be performed with electrodes placed in the external ear canal or on the surface of the tympanic membrane. The latter is gaining in popularity because of ease of placement and the clarity and amplitude. This electrode is positioned gently onto the central portion of the lateral surface of the TM under microscopic visualization. Recording from the external auditory meatus skin (EAM) can be accomplished with an expanding leaf-type surface electrode or a foam insert ear phone covered with gold foil. Although these electrodes are simple to place, the response amplitudes are considerably degraded and the noise levels are higher compared with TM electrodes.



(a)



(b)



(c)

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ELECTROCOCHLEOGRAPHY

ELECTROCOCHLEOGRAPHIC ABNORMALITIES IN PATIENTS WITH MD

ECochG is often used in the clinical investigation of hydrops conditions of the cochlea, such as MD, but its diagnostic utility and interpretation remain topics of controversy. It is believed that the presence of hydrops increases the amplitude of the SP by affecting the elasticity and resting position of the basilar membrane.. Endolymphatic hydrops is associated with relatively larger SP/AP values. Most investigators have used a value of 0.3 to 0.4 as the upper limit of normal for SP/AP, and have found that approximately two-thirds of MD ears have abnormal ECochG results. Only 76% of patients with MD had abnormal ECochG ²².

DEHYDRATION TESTING

The most distinctive test is the Glycerol dehydration test in which the patient is made to ingest glycerol (1.5 cc/kg of body weight) and the air-conduction audiometric test is repeated at every half to 1 hour intervals. If the patient suffers from Meniere's disease then an improvement of hearing level will be obtained by 10-15 dB in most frequencies, especially the lower frequencies. For the glycerol test to be considered as positive there should be a hearing improvement of at least 5 dB in three consecutive octaves. This improvement of hearing threshold occurs due to the dehydrating effect of the glycerol, on the endolymphatic fluid in the inner ear. The dehydration brought about by the glycerol decreases the volume of the endolymph and reverses the hydrops which improves the hearing.

Side effects may include headache, nausea, dizziness, diarrhea, thirst, emesis, and diuresis ²¹.

MEDICAL THERAPY FOR MENIERE’S DISEASE

Treatment of acute exacerbations

Acute attack of Meniere’s disease is characterized by acute rotational vertigo, transient fluctuations in hearing, tinnitus, and aural fullness. Initial management focuses on excluding other conditions that can present with same symptoms, including vestibular neuritis, migraine, cerebral vascular events, multiple sclerosis and tumors. Acute management of Meniere’s disease is mainly symptomatic control. Vestibular suppressants can be used ⁷.

Low-salt diet and lifestyle modification

It has been believed that a high salt diet can influence the osmotic gradients in the inner ear. Levels of salt restriction range from 2g per 24hrs down to 1g per 24hrs. There is no strong evidence exists to support the role of salt restriction alone in reducing the frequency or severity of symptoms from Meniere’s disease.

Diuretics

Diuresis reduces the amount of endolymphatic hydrops by reducing the extracellular fluid in the body. Hydrochlorothiazide is perhaps the most widely advocated, although frusamide and spiranolactone have their supports. There is no clear scientific evidence exists to support their efficacy.

Betahistine

Cochlear vascular insufficiency as a result of autonomic dysfunction has been proposed as a cause of MD. Betahistine has been proposed as a treatment because of its theoretic vasodilatory effects on the blood supply to the inner ear. The betahistine have weak H₁-receptor agonistic and considerable H₃-

antagonistic properties in the central nervous system and autonomic nervous system. Many of these trials found betahistine to be effective in reducing the frequency in severity of vertiginous episodes and to some extent helping with tinnitus. No evidence exists to show betahistine helps with symptoms of hearing loss ²³.

Corticosteroids

The steroid perfusion can influence the sodium and fluid dynamics in the inner ear because their mineralocorticoid property. Potential advantages of steroid use include the low risk of complication and potential beneficial of hearing ²⁴.

Meniett device

Meniett device is a minimally invasive, nondestructive therapy. Its use is based on the observation that pressure changes applied to the inner ear result in beneficial changes in the symptoms of patient. The patient requires a standard ventilation tube to be placed before use. The Meniett device applies pulses of pressure to the inner ear via the ventilation tube. A treatment cycle takes 5 minutes and is repeated 3times a day. Meniett device is a second line therapy when first line medical therapy failed ²⁵.

Gentamicin perfusion

In the 1990s, gentamicin perfusion/ injection emerged as a predominant therapy for the incapacitating of vertigo of Meniere's disease. Gentamicin is an amino glycoside antibiotic that is preferentially toxic to the dark cell and hair cell (not so much) of the vestibular labyrinth. A variety of techniques have been developed to ablate the diseased labyrinth with intra tympanic gentamicin.

Dosage schedules and routes of administration vary considerably according to technique.

The patient is placed in the trendelenberg position with the affected ear turned up and head turned at a 45 degree angle. The posterior aspect of the tympanic membrane is anesthetized using a drop of phenol and a gentamicin solution (either a solution buffered with sodium bicarbonate with a gentamicin concentration of 30mg/cc or unbuffered solution with a gentamicin concentration of 40mg/cc) is injected by fine needle. The entire posterior half of the tympanic cavity filled with gentamicin, the creation of a pinpoint tympanic membrane perforation anterior to malleus allowing air escapes this process. The patient is left in position for 45 minutes and then discharged, with instruction to return in 1 week for a second injection.

In the majority of cases, two injections suffice to episodic vertigo. If the vertigo persists and there is no hearing loss, additional injection is performed.

The therapy is recommended only in unilateral Meniere's disease. The amount of gentamicin that leaks down the Eustachian tube and is lost nasopharynx, escapes back to the external canal. The degree of hearing loss depends not only on the total dose and dose schedule, but also on the susceptibility of the individual to gentamicin.

The advantages of gentamicin injection are clear. At least first several years, the procedure seems to achieve a vertigo control similar to that of vestibular neurectomy, without associated morbidity and mortality ^{9,6}.

SURGICAL MANAGEMENT

Surgery for can be divided into auditory-sparing (conservative) and auditory- ablative (destructive) procedures. There are several procedures of historical interest that are no longer in general use.

Sacculotomy

1964, Fick recommended puncture of the stapes foot plate with a sharp needle to rupture the under laying saccule. The procedure used a transcanal approach, with the elevation of a tympanomeatal flap. Long term follow up has revealed a considerable incidence of progressive hearing loss.

Cochleosacculotomy

This approach is the permanent fistulization of the endolymphatic and perilymphatic spaces were devised by House (the otic – periodic shunt). The procedure was performed via an exploratory tympanotomy approach. In the otic-periotics shunt procedure, a tube was placed through the round window membrane to perforate the basilar membrane. In the cochleosacculotomy, a right angle hook was inserted through the round window membrane so as to cause a fracture /dislocation of the osseous spiral lamina. High incidence of sensorineural deafness, these procedures is rarely performed.

Endolymphatic Sac Surgery

Endolymphatic sac decompression or drainage has been espoused for the management of endolymphatic hydrops since portmann's in 1926. The procedure begins with a simple mastoidectomy with identification of the middle and posterior fossa dural plates, sinodural angle, sigmoid sinus, antrum, the horizontal semicircular canal and incus. Using a diamond bur, the facial nerve is

identified leaving intact a thin bony covering from the horizontal canal to the stylomastoid foramen. The visualization of the facial nerve enables safe removal of the retrofacial cells and identification of the endolymphatic sac. The posterior semicircular canal is next identified. Once the posterior canal has been identified, the posterior fossa dural plate is removed between the sigmoid sinus and the posterior canal. The endolymphatic sac is located by tracing an imaginary **(Donaldson's) line** through the horizontal semicircular canal, perpendicular to and bisecting the posterior semicircular canal. Edge of the endolymphatic sac is usually located just inferior to this line. The precise management of the sac subsequent to its identification varies according to which procedure is conducted ¹⁰.

In decompression of the sac, removal of all bone of the posterior fossa dural plate completes the procedure. Attempts to revascularize the decompressed sac with a temporalis muscle pedicle flap have been abandoned. Shunting of the sac can be performed either into the mastoid or the subarachnoid space. House developed the endolymphatic subarachnoid shunt procedure, in which both walls of the endolymphatic sac are incised, and a specially designed silicone (Silastic) shunt tube is inserted into the lateral prolongation of the basal cistern.

Labyrinthectomy

A cortical mastoidectomy is performed. The posterior external bony canal wall is thinned, the bone over the tegmen is thinned, and the sigmoid sinus is skeletonized. The labyrinth is skeletonized and the cells of the mastoid tip are opened. The labyrinthectomy is performed by opening of the lateral semicircular canal. The lateral canal is only half opened to canal and following to the posterior protect the external genu of the facial nerve. The posterior canal, having been opened, can be traced to its confluence with the superior

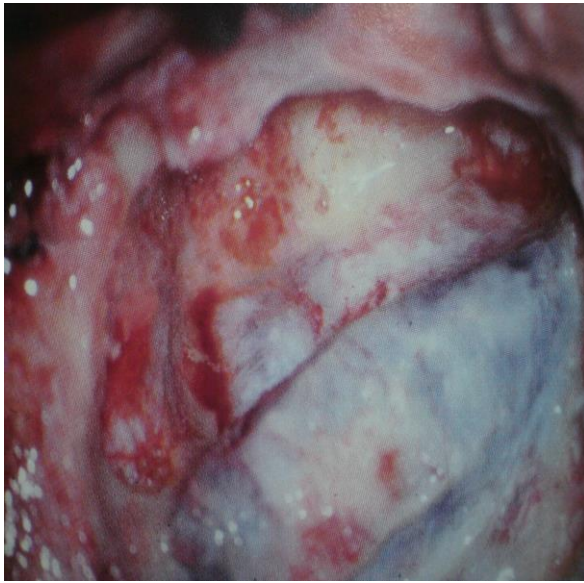
semicircular canal, where the two canals combine to become the common crus. The common crus may then be followed directly forward to the vestibule. With all the canals and the vestibule opened, all soft-tissue elements of the membranous labyrinth should be removed.

Translabyrinthine Vestibular Neurectomy

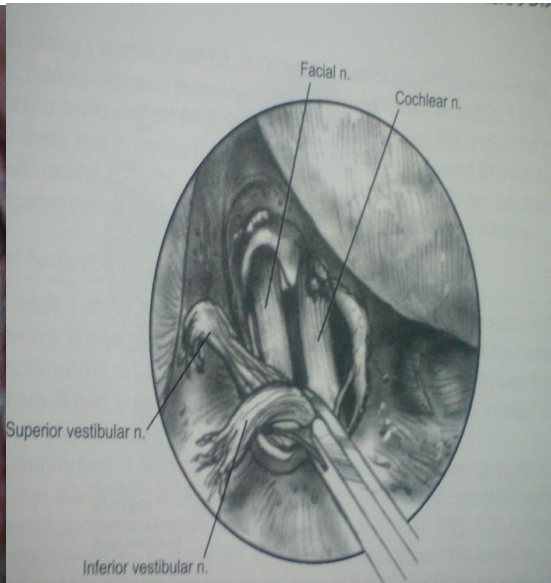
Mastoidectomy and labyrinthectomy are performed as previously described under labyrinthectomy. Exploration of the IAC is clear identification of the IAC contents. When dissecting the AC is to enable identification of the facial nerve in its normal position and extend the dissection into the diseased area.

Once the IAC is adequately skeletonized, the thin bone over the canal is lifted away with a small right-angle pick. The perforated area where the superior vestibular nerve enters both the lateral and the superior ampullae is thinned carefully, and a 1-mm hook is used to avulse the superior vestibular nerve from the vestibular nerve recess that it makes in the labyrinthine bone lateral to the fallopian canal. As the superior vestibular nerve is reflected, the facial nerve comes into view deep to the plane of dissection.

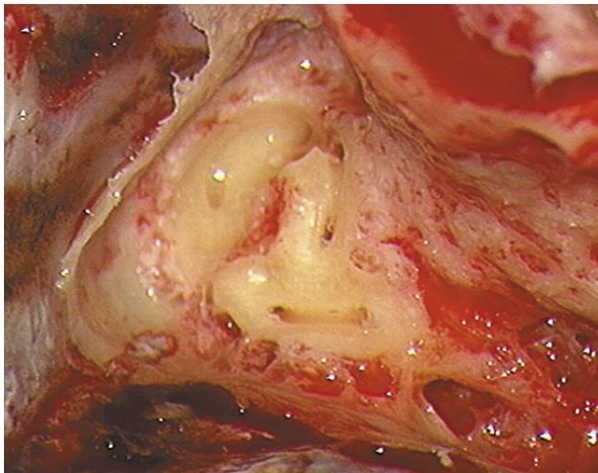
With the superior vestibular nerve separated from the facial nerve, the inferior vestibular nerve is also avulsed with the singular nerve to the posterior semicircular canal. Failure to include the singular nerve may cause failure of the operation ²⁰.



Endolymphatic sac decompression



Vestibular nerve section



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Labyrinthectomy

MATERIALS

This study was a prospective study. Institutional ethical committee clearance was obtained for the study. During the study period Jan 2010 to Nov 2010, the patients attending the outpatient department of the Upgraded Institute of Otorhinolaryngology, Madras Medical College & Government General Hospital, and Chennai were screened for Meniere's disease. These patients were explained about the study. Those who have given consent were included in the study as per inclusion and exclusion criteria.

INCLUSION CRITERIA:

People attending neuro – otologic clinic were classified into Very definite and Definite Meniere's disease according to AAO HNS classification

AAO-HNS CLASSIFICATION

VERY DEFINITE MERIERE'S DISEASE

- The patient has had at least two attacks of sudden vertigo has lasted more than 20 minutes but less than a day along with Deafness, Tinnitus, Aural fullness, Glycerol dehydration test positive , EcochG positive

DEFINITE MENIERE'S DISEASE;

- Episodic vertigo, Deafness, Tinnitus, Aural fullness, Positive glycerol positive test, Typical EcochG finding not present

Both male and female, age > 15 years

EXCLUSION CRITERIA:

People with previous ear disease like CSOM, congenital malformation,

People with previous ear surgeries, syphilis, intracranial tumour

People on ototoxic drugs, head injury, any other major exanthematous illness

People with positive family history of HOH

SAMPLE SIZE: 50**CONTROL GROUP**

The patients were attending neuro-otologic clinic with symptoms of Meniere's disease. The patient is treated with oral betahistine.

METHODOLOGY

The Patients who attend the neuro otologic clinic with vertigo ,tinnitus, fluctuate hearing loss for which to confirm Meniere's disease by audiogram , glycerol test ,tone decay, SISI, ECochG.

Before doing glycerol test, the basic investigations like blood sugar, urea and ECG to be done and to avoid glycerol complication.

The patient should get anesthetist fitness, before going to the procedure.

The patient is placed in the trendelenberg position with the affected ear turned up and head turned at a 45 degree angle. The posterior canal wall is anesthetized with 2% xylocaine. The ventilation tube is inserted in the posterior inferior quadrant of the tympanic membrane.

0.7ml of gentamicin(0.7ml=30mg/) mixed with 0.3ml of sodium bi carbonate solution is injected intratympanically once a week for 3 consecutive weeks. If the patient came with complaints of hearing impairments after the first dose, the next dose should be avoided.

After 6 months of intratympanic gentamicin therapy, patient has to be evaluated using ECochG and audiogram. Patient has to be graded according to AAO - HNS criteria of vertigo control and hearing level changes.

Numeric value scale	control level	class
0	complete control of definitive spells	A
41-80	limited control of definitive spells	B
81-120	insignificant control of definitive spells	C

>120

D

Secondary treatment initiated

E

Hearing classification:

- Unchanged=10d B PTA ,15% SD
- Improved >10 d B PTA >15% SD
- Worse >10 d B PTA worsened >15% SD worsened.

The control group is also confirmed by glycerol test, ECochG.

Statistical analysis was made using ANOVA and Paired 't' Test

RESULTS & ANALYSIS

Observation of 50 patients who underwent intratympanic gentamicin therapy is as follows.

AGE AND SEX DISTRIBUTION

Age of the patients participated in this study and control is from 15 to 60 years.

Table 1 Age Distribution

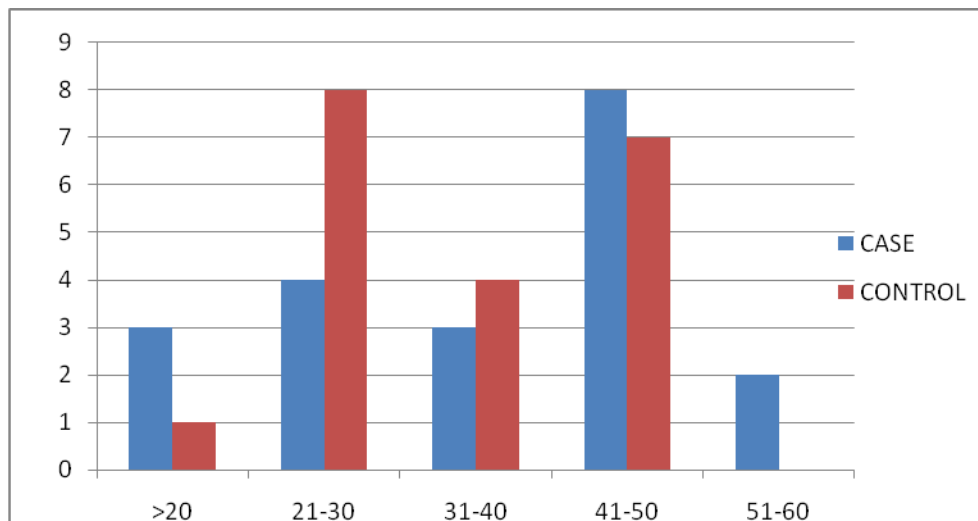
AGE	CASE	%	CONTROL	%
<20	3	15	3	10
21-30	4	20	13	43
31-40	3	15	6	20
41-50	8	40	8	27
51-60	2	10	0	0

In sex distribution 55% to 60% is male and 43% to 45% is female.

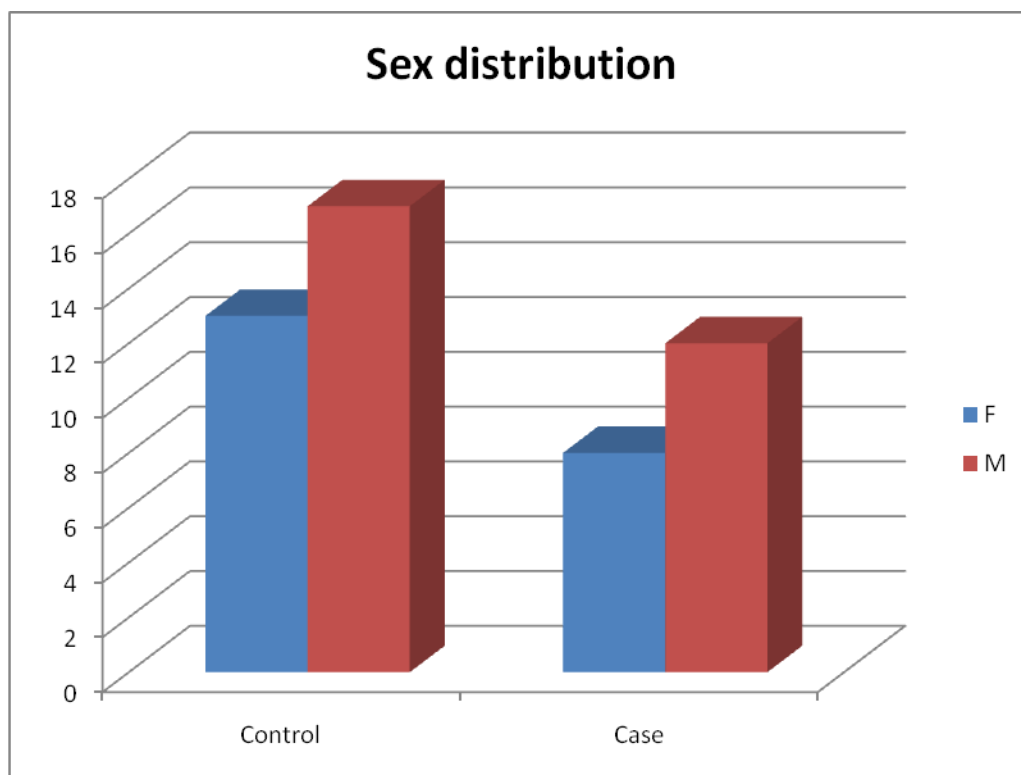
Table 2 Sex Distribution

Sex	Control		Case		Total
	Count	%	Count	%	
F	13	43.3	8	40.0	21
M	17	56.7	12	60.0	29
Total	30	100.0	20	100.0	50

p = 0.984 Not Significant



AGE DISTRIBUTION



SEX DISTRIBUTION

CLASSIFICATION

The study and control group are classified into very definitive and definitive Meniere's disease by glycerol test and ECochG.

Table 3 Classification

Classification	Control		Case		Total
	Count	%	Count	%	
Definite	13	43.3	7	35.0	20
Very definite	17	56.7	13	65.0	30
Total	30	100.0	20	100.0	50

$p = 0.769$

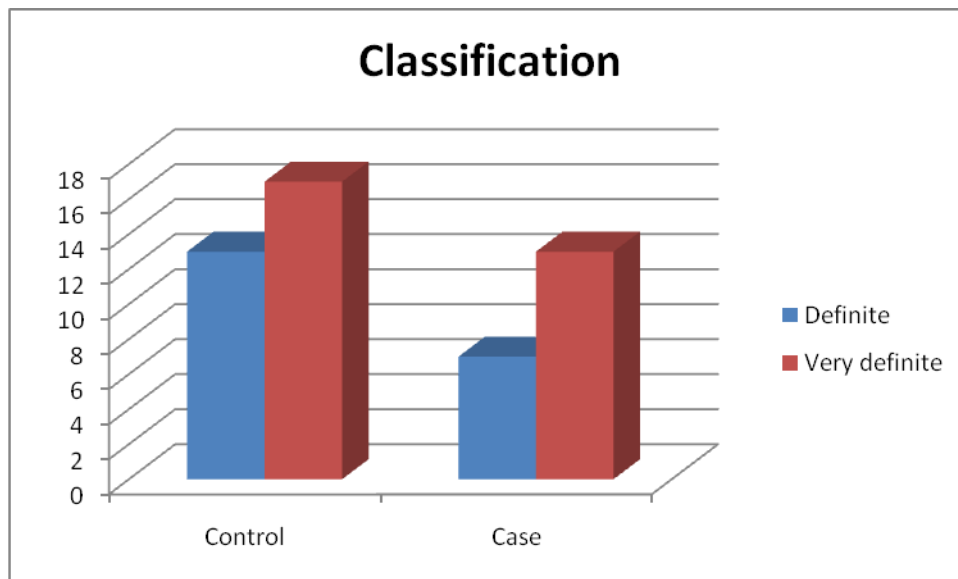
STAGING

According to symptoms and hearing level the case and control are divided into 4 stages.

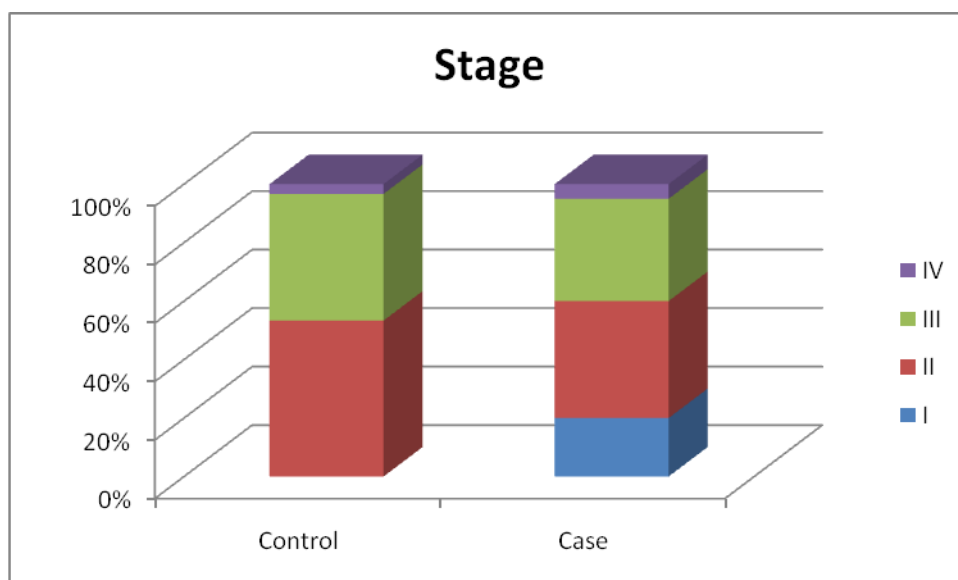
Table 4 Staging

Stage	Control		Case		Total
	Count	%	Count	%	
I	0	0.0	4	20.0	4
II	16	53.3	8	40.0	24
III	13	43.3	7	35.0	20
IV	1	3.3	1	5.0	2
Total	30	100.0	20	100.0	50

$p = 0.081$



CLASSIFICATION



STAGING

GLYCEROL TEST

The glycerol test is positive in side of the ear of both cases and controls.

Table 5 Glycerol Test

Glycerol Test	Control		Case		Total
	Count	%	Count	%	
Lt++Ve	14	46.7	9	45.0	23
Rt++Ve	16	53.3	11	55.0	27
Total	30	100.0	20	100.0	50

P=0.998

ELECTROCOCHLEARGRAM

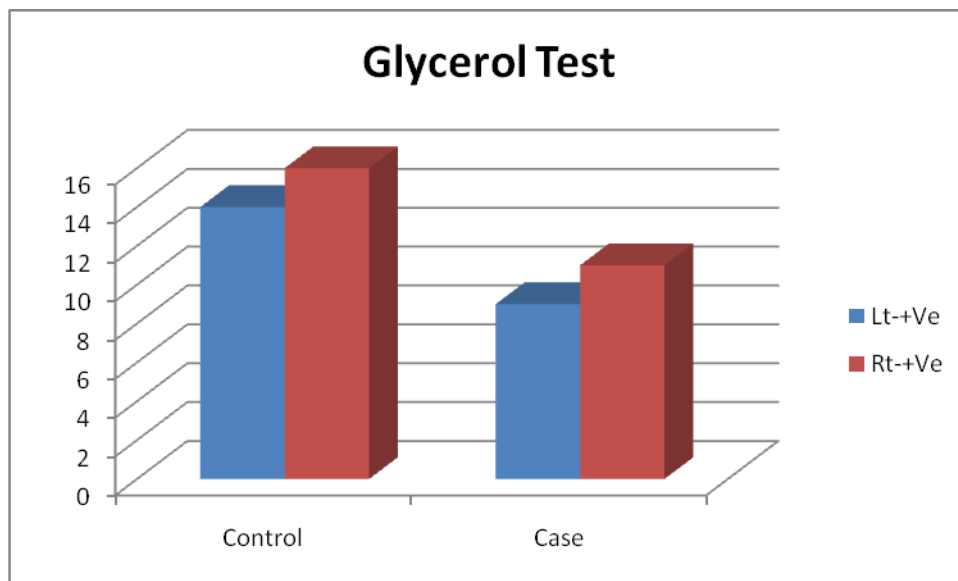
Both pre operative and post operative ECoChG are taken. In the control group only pre treatment ECoChG are taken.

Table 6 Pre operative and post operative ECoChG

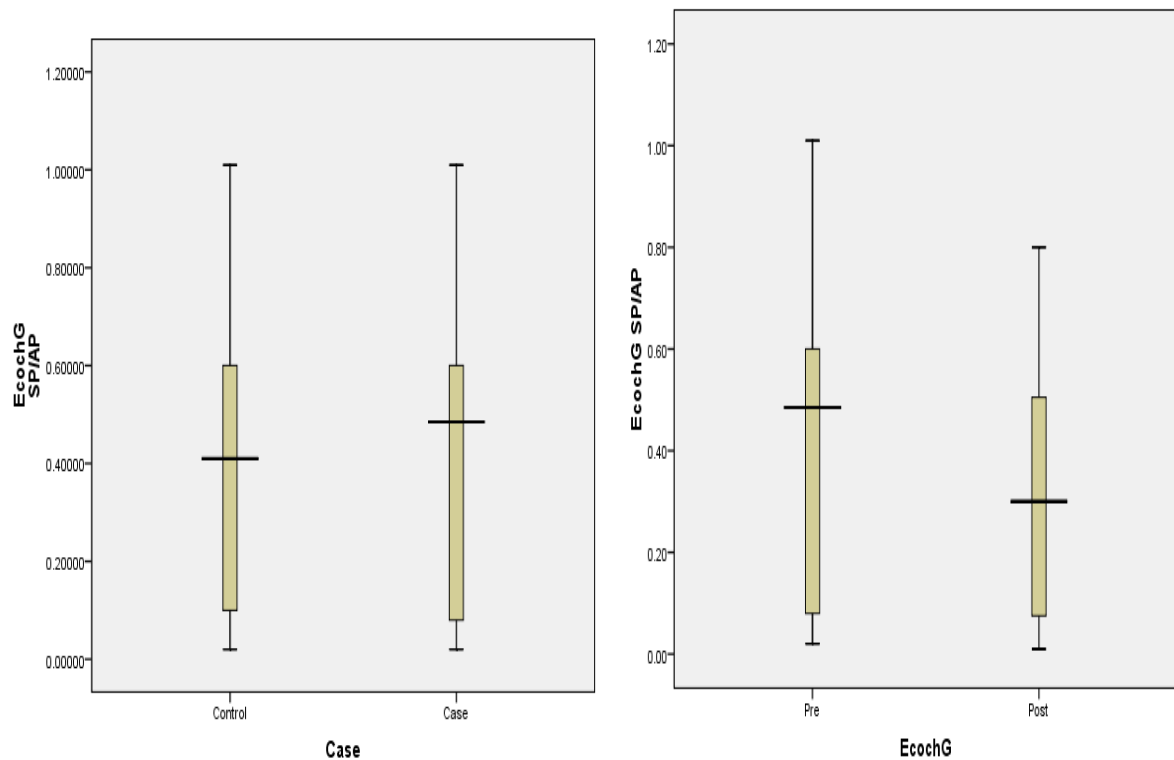
EcochG SP/AP			Post op EcochG			t	Df	p value
Mean	N	S D	Mean	N	S D			
0.43	20	0.29	0.328	20	0.24	3.82	19	0.001

Table 7 Case vs Control

	Case			Control			T	Df	p value
	N	Mean	S D	N	Mean	S D			
EcochG SP/AP	20	0.43	0.29	30	0.40	0.28	0.30	48	0.768



Glycerol Test



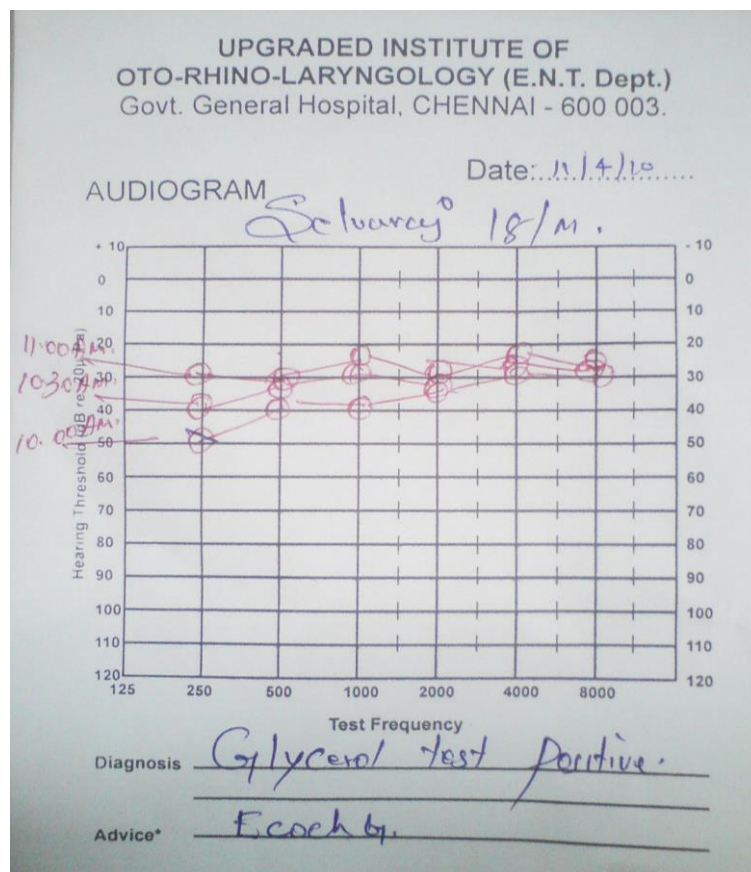
**BOX-PLOT Curve comparing Case vs Control and the Pre-op and Post-op
EcochG in the Case group**

Table 8 Case Summaries

Case	Age	EcochG SP/AP	Post op EcochG
Control	N	30	
	Mean	32.40	.40
	Std. Deviation	10.759	.285
	Minimum	18	0
	Maximum	50	1
Case	N	20	20
	Mean	37.10	.43
	Std. Deviation	12.578	.239310
	Minimum	17	.010
	Maximum	57	.800
Total	N	50	20
	Mean	34.28	.41
	Std. Deviation	11.630	.239310
	Minimum	17	.010
	Maximum	57	.800



ELECTROCOCHLEOGRAPHY



GLYCEROL TEST

VERTIGO CONTROL

After 6 months of therapy, both case and control are clinically evaluated by AAO-HNS guidelines.

Table 9 Vertigo Control

Vertigo Control	Control		Case		Total
	Count	%	Count	%	
A	9	30.0	12	60.0	21
B	12	40.0	7	35.0	19
C	5	16.7	0	0.0	5
D	4	13.3	0	0.0	4
E	0	0.0	1	5.0	1
Total	30	100.0	20	100.0	50

p = 0.038 Significant

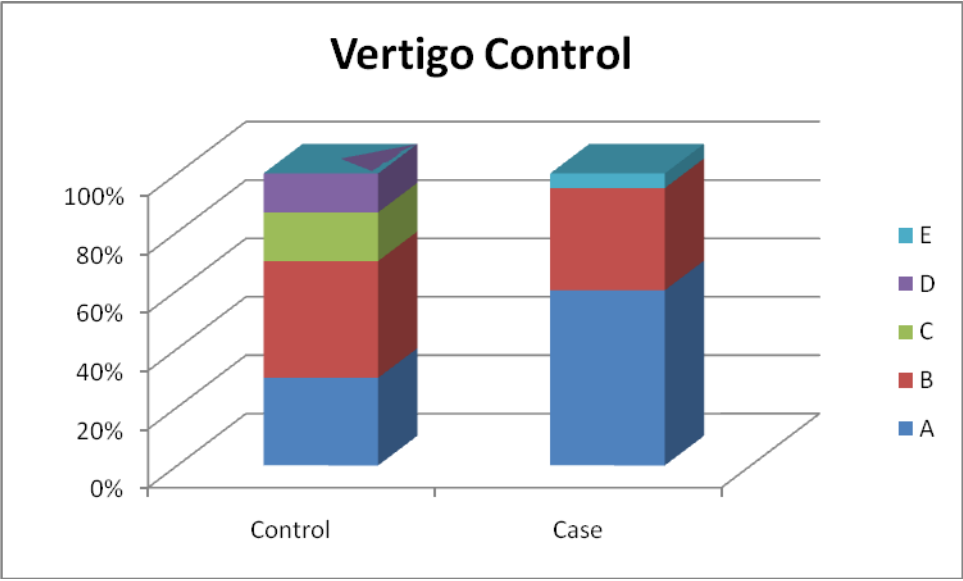
HEARING LEVEL CONTROL

Both case and control are evaluated by audiogram.

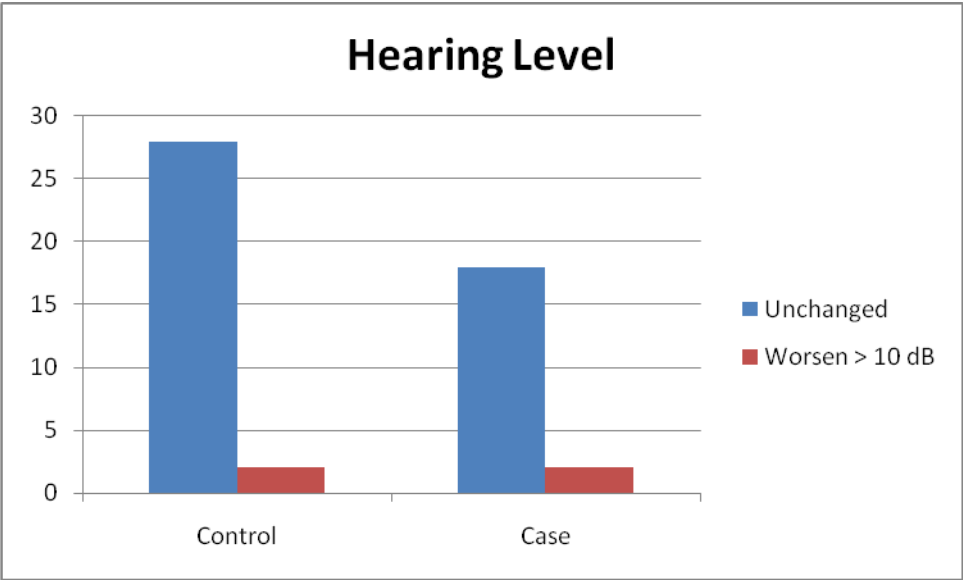
Table 10 Hearing level

Hearing Level	Control		Case		Total
	Count	%	Count	%	
Unchanged	28	93.3	18	90.0	46
Worsen > 10 dB	2	6.7	2	10.0	4
Total	30	100.0	20	100.0	50

p = 0.987



Vertigo Control



Hearing Level

DISCUSSION

Despite many years of research, the exact cause of MD remains elusive. Medical management is the mainstay of treatment of MD. Further research is required to evaluate the effect of treatments. Chemical labyrinthectomy using aminoglycosides is an effective alternative to second line treatment for those patients in whom medical management is unsuccessful.

This study of 20 case and 30 control patient over the period from Jan 2010 to Nov 2010. They included in the case group 40% of male and 60% of female, like wise in the control group 56.7% of male and 43.3% of female.

The patient came with episodic vertigo, fluctuating hearing loss, aural fullness and tinnitus were included in the study, and they were staged by their symptom and audiogram.

In both the study group and the control group the patient presented maximum at Stage II. Though none of the study population belonged to Stage I, in comparison to 20 % of the control population, this was not statistically significant ($p=0.08$)

The study and control group were diagnosed into very definitive and definite Meniere's disease by glycerol test and ECochG

In this study 65% of patient was diagnosed very definitive Meniere's disease and 35% was diagnosed definitive Meniere's disease. In the control group 55% of the patient was diagnosed very definitive Meniere's disease and 45% of the patient was diagnosed definitive Meniere's disease.

The study group was treated with intratympanic gentamicin therapy 3 times at weekly interval, while the control group was treated with oral betahistine.

At the end of the study period ECoChG was taken for the study group and 54% of patient reverted to normal ECoChG.

In the study group 90% of patient showed no changes in hearing level, and 10% of patient showed worsening of hearing level. This was insignificant when compared to the control group. ($p=0.987$)

In the study group, the patient was in vertigo control level A 60%, B 35% and E 5% ($n=1$) of patient had gone for secondary surgical management. In the control group, the patient was in vertigo control level A 30%, B 40%, C 16.7%, D 13.3% which was significant ($p=0.038$) suggesting a better vertigo control in the cases.

In the US study, Kaasinen and colleagues were one of the first groups to publish a large series in which the AAO-HNS guidelines were followed. A total of 93% patients treated with transtympanic gentamicin for MD. Rotatory vertigo was abolished in 81% of patients treated. 10% patients suffered dead ears as a response to treatment, and mean pure tone average decreased by 8.8 dB.

Cohen-kerem and colleagues under look a meta-analysis that combined the result of 15 trials in which the AAO-HNS guidelines for reporting treatment results in MD were used. This analysis represented 627 patients. Class A vertigo control was achieved in 74.7% of patients and class B in 92.7% of patient.

In articles reporting results from patient treated with fixed dose protocol, the overall success rate was 68.7% for class A control and 91.9% for class B control.

Driscoll and colleagues using a treatment regimen consisting of a single gentamicin injection, result of short term control of vertigo in 85%, with a 5 to 10% acute hearing loss related to injection (4).

A larger series consisting of 90 patients, using the same treatment regimen, was published in 1996. A total of 85% of patients reported complete vertigo control and 9% reported substantial vertigo control. Hearing loss occurred in 23% of patients; 165 of patients suffered a severe to profound hearing loss which was contradictory to our research which showed only a statistically insignificant 10% (n=2)

The most recent study, in which the minimum follow-up time after treatment was 5 years and the average follow-up time was 15.5 years, again showed consistently good vertigo control.

Thus my study showed a vertigo control of 60% relatively the same as above mentioned studies which showed a vertigo control of 60 to 75%.

In my study 10% of patients showed worsening of hearing level while the above mentioned studies showed 10-23% worsening of hearing level.

CONCLUSION

In this study 60% of patients were diagnosed with very definite Meniere's disease and 40% of patients were diagnosed definite Meniere's disease using ECoChG.

In this study 60% of patients showed improvements of vertigo control with intratympanic gentamicin therapy, while in control group only 30% of patients showed improvements.

My study shows that intratympanic gentamicin therapy is more effective in controlling vertigo in Meniere's disease patients.

Post intra tympanic gentamicin therapy ECoChG was significantly improved.

In this study 10% of patients showed worsening of hearing level with intratympanic gentamicin therapy, while in 6.7% of patients showed worsening of hearing with oral therapy.

BIBLIOGRAPHY

1. Kimmura R. Distribution, structure and function of dark cells in the vestibular labyrinth. *Annals of otology, rhinology, laryngology* 1969; 78: 542-61
2. Dohlman G. Mechanism of the meniere attack. *ORL; Journal for oto-rhino-laryngology*: 1980; 42:10-19
3. Youssef TF, Poe DS. Intra tympanic gentamicin injection for the treatment of Meniere's disease *Am J otol* 1998; 19:435-42
4. Driscoll CL, Harner SG, et al. Low dose intratympanic gentamicin and the treatment of Meniere's disease, *Laryngoscope* 1997; 197:83-9
5. Kaplan DM, Intratympanic gentamicin for the treatment of unilateral Meniere's disease. *Laryngoscope* 2000; 110:1298-305
6. Harner SG, Driscoll CL, Facer W, et al. long term follow-up transtympanic gentamicin for Meniere's disease. *Otol Neurotol* 2001; 22:210-4.
7. Perez N, Martin E, Gargia-Tapia R. Intra tympanic gentamicin for intractable menere's disease. *Laryngoscope* 2003; 113:456-64.
8. Wu IC, Minor LB. Longterm hearing outcome in patient receiving intratympanic gentamicin for Meniere's disease *Laryngoscope* 2003; 113:815-20.
9. Bodmer D, Morong S, Stewart C, ET akl. Long term vertigo control in patients after intratympanic gentamicin instillation for Meniere's disease. *Otol Neurotol* 2007; 28:1140-4.

10. Paparella MM, Hanson DG. Endolymphatic sac drainage. *Laryngoscope* 1976; 86:697-703.
11. Derlacki EL. Non surgical management of Meniere's disease. *Laryngoscope* 1954; 64:271-82.
12. Hallpike CS, Carins HWB. Observations of the pathology of Meniere's syndrome. *Proc R Soc Med* 1938; 31:1317-36.
13. Schuknecht HF. Histopathology of Meniere's disease. In: Harris JP, editor. *Meniere's disease*. The Netherlands: Kugler; 1999. p.41-52.
14. Merchant SN, Adams JC, and Nadol JB Jr. pathophysiology of Meniere's syndrome: are symptoms caused by endolymphatic hydrops? *Otol Neurotol* 2005; 26:74-81.
15. Yoon TH, Paparella MM, Schachern PA, et al. Cellular changes in Reissner's membrane in endolymphatic hydrops. *Ann Otol Rhinol Laryngol* 1991; 100:288-93
16. Horner Kc. Review: morphological changes associated with endolymphatic hudrops. *Scanning Microsc* 1993; 7:223.
17. Schuknecht Hf. Meniere's disease: a correlation of symptomatology and pathology. *Layngoscope* 1963; 73:651.
18. Tsuji K, Velazquez-Villasenor L, Rauch SD, et al. Temporal bone studies of the human peripheral vestibular system. Meniere's disease. *Ann Otol Rhinol Laryngol Suppl* 2000; 181:26.

19. Honrubia V. Pathophysiology of Meniere's disease: vestibular system. In: Harris JP, editor. Meniere's disease. The Hague: Kugler Publications; 1999.p.231.
20. Fisch U. Vestibular and cochlear neurectomy. Ophthalmol otolaryngol. 1974; 78:252-60.
21. Andersen H, Bingel U, Streichert T, et al. severe glycerol intoxication after Meniere's disease diagnostic- clin toxicol 2009;47 (4):312.
22. Devaian AK, Dawsen KL, Ferraro JA , et al utility of area curve ratio electrocochleography in Meniere's disease. Arch otolaryngol head neck surgery 2003;129(5):547-51.
23. Wilmot TJ, Menon GN. Betahistine in Meniere's disease. J laryngology otol 1976;90:833-40.
24. Shea JJ, Ge X. dexamethasone perfusion of the labyrinth for Meniere's disease. Otolaryngol clin north am 1996;29:353-9.
25. Mattox DE, Rechiert M. meniett device for Meniere's disease: use and compliance at 3 to 5 years. Otol neurotol 2007;29:29-32.

PROFORMA

DATE:

NAME:

AGE:

SEX: M/F OP NO

ADDRESS:

OCCUPATION:

STUDY NO:

Presenting Complaint:

Giddiness

Unsteadiness

HOH

Tinnitus

Headache

Examination:

HOH

Tinnitus

Ears:

Duration

Nose:

Side

Throat:

Sudden

Fistula Test:

Progressive

Fluctuating

Vestibular system:

INVESTIGATIONS:

BLOOD SUGUR, UREA, X-RAY CHEST, ECG

PURE TONE AUDIOGRAM

TONE DECAY, SISI,

GLYCEROL TEST

ELECTROCOCHLEOGRAPHY STAGE: CLASSIFICATION:

POST GENTAMICIN THEREPY

ELECTROCOCHLUOGRAPHY, AUDIOGRAM, HEARING LEVEL:
VERTIGO CONTROL:

ABBREVIATION

MD	-	MENIERE’S DISEASE
SISI	-	SHORT INCRIMATION SENSITIVE INDEX
CPA	-	CEREBELLO PONTINE AGCLE
SD	-	SPEECH DISCRIMINATION
PTA	-	PURE TONE AVERAGE
VOR	-	VESTIBULO OCULAR REFLEX
SP	-	SUMMATION POTENTIAL
AP	-	ACTION POTENTIAL
CM	-	COCHLEAR MICROPHONY
VEMP	-	VESTIBULAR EVOKED MYOGENIC POTENTIAL
SISI	-	SHORT INCREMENT SENSITIVITY TEST
ABLB	-	ALTERNATE BINAURAL LOUDNESS BALANCE TEST
TDT	-	TONE DECAY TEST
SCM	-	STERNOCLEDO MASTOID
EAM	-	EXTERNAL AUDITORY MEATUS
TM	-	TYMPANIC MEMBRANE

S.No	Name	Case	Age	Sex	OP No	Classification	Stage	PTA	Glycerol Test	Special Test	EcochG SP/AP	op Post EcochG	Vertigo Control	Hearing Level
1	Selvaraj	1	25	M	20404	Very definite	II	Lt-32dB	Lt-+Ve	TDT- Ve SISI 70%	0.60	0.32	A	Unchanged
2	Vishalatchi	1	41	F	22135	Definite	III	Rt-46dB	Rt-+Ve	TDT- Ve SISI - 90%	0.05	0.05	B	Unchanged
3	Kandhan	1	19	M	52075	Definite	II	Lt-28dB	Lt-+Ve	TDT- Ve SISI - 80%	0.04	0.04	A	Unchanged
4	Kanthurubi	1	50	F	10378	Very definite	III	Rt-52dB	Rt-+Ve	TDT- Ve SISI - 70%	0.70	0.70	E	Worsen > 10 dB
5	Manimagalai	1	32	F	90701	Very definite	II	Rt-30dB	Rt-+Ve	TDT- Ve SISI - 70%	0.60	0.29	A	Unchanged

6	Thulasi Bai	1	48	F	13843	Definite	III	Lt-50dB	Lt-+Ve	TDT- Ve SISI - 70%	0.02	0.01	B	Unchanged
7	Vediyammal	1	28	F	7049	Very definite	III	Lt-45dB	Lt-+Ve	TDT- Ve SISI - 70%	0.60	0.60	A	Unchanged
8	Rani	1	40	F	25933	Very definite	III	Rt-48dB	Rt-+Ve	TDT- Ve SISI - 100%	0.50	0.40	B	Unchanged
9	Alagiri	1	52	M	8092	Definite	IV	Lt-64dB	Lt-+Ve	TDT- Ve SISI - 70%	0.03	0.03	B	Worsen > 10 dB
10	Sunmugasundharam	1	50	M	38214	Very definite	II	Lt-40dB	Lt-+Ve	TDT- Ve SISI - 70%	0.80	0.60	A	Unchanged
11	Tamilarasu	1	17	M	12267	Very definite	I	Rt-24dB	Rt-+Ve	TDT- Ve SISI - 70%	0.47	0.30	A	Unchanged
12	Sakil Ahmed	1	45	M	12671	Definite	II	Lt-35dB	Lt-+Ve	TDT- Ve SISI - 70%	0.06	0.04	A	Unchanged

13	Rajendran	1	41	M	8322	Very definite	I	Rt-22dB	Rt-+Ve	TDT-Ve SISI - 70%	1.01	0.80	B	Unchanged
14	Mani	1	40	M	25933	Definite	II	Rt-34dB	Rt-+Ve	TDT-Ve SISI - 100%	0.10	0.10	A	Unchanged
15	Nirmal Raj	1	45	M	2401	Very definite	I	Rt-16dB	Rt-+Ve	TDT-Ve SISI - 100%	0.49	0.30	A	Unchanged
16	Meera	1	57	F	12238	Definite	II	Rt-32dB	Rt-+Ve	TDT-Ve SISI - 70%	0.29	0.29	B	Unchanged
17	Senthil	1	21	M	8749	Very definite	I	Rt-18dB	Rt-+Ve	TDT-Ve SISI - 100%	0.60	0.30	A	Unchanged
18	Stalin	1	25	M	9944	Very definite	II	Lt-34dB	Lt-+Ve	TDT-Ve SISI - 80%	0.47	0.41	A	Unchanged
19	Kasturi	1	46	F	12801	Very definite	III	Lt-52dB	Lt-+Ve	TDT-Ve SISI - 70%	0.60	0.60	B	Unchanged

20	Gopalakrishnan	1	20	M	26075	Very definite	III	Rt-55dB	Rt-+Ve	TDT-Ve SISI - 80%	0.48	0.38	A	Unchanged
1	mohammed ansari	0	37	m	2074	Definite	II	Rt-30dB	Rt-+Ve	TDT-Ve SISI 70%	0.30		A	Unchanged
2	manika valli	0	46	f	4801	Definite	II	Rt-28dB	Rt-+Ve	TDT-Ve SISI >60%	0.05		B	Unchanged
3	kumeresan	0	24	m	2083	Very definite	III	Lt-40dB	Lt-+Ve	TDT-Ve SISI >60%	0.40		C	Worsen > 10 dB
4	Natarajan	0	44	m	4056	Very definite	II	Lt-18-Db	Lt-+Ve	TDT-Ve SISI - 70%	0.70		B	Unchanged
5	Neela	0	50	f	3181	Definite	II	Rt-30dB	Rt-+Ve	TDT-Ve SISI - 70%	0.31		A	Unchanged
6	john kennedy	0	48	m	3089	Definite	III	Lt-50dB	Lt-+Ve	TDT-Ve SISI - 60%	0.02		C	Unchanged

7	kurshith	0	50	m	4178	Very definite	II	Rt-26dB	Rt-+Ve	TDT-Ve SISI - 60%	0.60		A	Unchanged
8	chinnaponnu	0	30	f	1086	Definite	IV	Lt-56dB	Lt-+Ve	TDT-Ve SISI - 100%	0.21		B	Unchanged
9	valliammal	0	44	f	2481	Very definite	II	Rt-30dB	Rt-+Ve	TDT-Ve SISI - 60%	0.70		B	Unchanged
10	sethu	0	22	m	4186	Very definite	III	Lt-40dB	Lt-+Ve	TDT-Ve SISI - 60%	0.7		A	Unchanged
11	subash	0	33	m	2100	Very definite	II	Rt-24dB	Rt-+Ve	TDT-Ve SISI - 60%	0.42		B	Unchanged
12	hajeera	0	18	f	3319	Definite	II	Lt-22dB	Lt-+Ve	TDT-Ve SISI - 60%	0.06		B	Unchanged
13	divakar	0	21	m	2710	Very definite	III	Rt-46dB	Rt-+Ve	TDT-Ve SISI - 60%	1.01		D	Unchanged

14	Joonath	0	34	f	3789	Very definite	II	Lt-20dB	Lt-+Ve	TDT-Ve SISI - 100%	0.10		A	Unchanged
15	Rani	0	48	f	2121	Very definite	III	Rt-56dB	Rt-+Ve	TDT-Ve SISI - 100%	0.43		D	Unchanged
16	Mahesh	0	30	m	2801	Definite	II	Rt-26dB	Rt-+Ve	TDT-Ve SISI - 70%	0.29		B	Unchanged
17	inbasekaran	0	30	m	4329	Very definite	III	Rt-50dB	Rt-+Ve	TDT-Ve SISI - 100%	0.60		A	Unchanged
18	Kalyani	0	22	f	5544	Definite	II	Lt-34dB	Lt-+Ve	TDT-Ve SISI - 80%	0.04		C	Unchanged
19	Riswan	0	23	m	3415	Very definite	III	Lt-52dB	Lt-+Ve	TDT-Ve SISI - 70%	0.60		B	Unchanged
20	dhanalakshmi	0	38	f	1643	Definite	III	Rt-55dB	Rt-+Ve	TDT-Ve SISI - 80%	0.24		C	Unchanged

21	singaram	0	18	m	6086	Definite	III	Lt-40dB	Lt-+Ve	TDT- Ve SISI - 60%	0.7		A	Unchanged
22	jeevarathinam	0	36	m	26800	Very definite	II	Rt-24dB	Rt-+Ve	TDT- Ve SISI - 60%	0.42		B	Unchanged
23	manjula	0	18	f	43316	Definite	II	Lt-22dB	Lt-+Ve	TDT- Ve SISI - 60%	0.06		B	Unchanged
24	sanker	0	21	m	25890	Very definite	III	Rt-46dB	Rt-+Ve	TDT- Ve SISI - 60%	1.01		D	Unchanged
25	devi	0	34	f	9123	Very definite	II	Lt-20dB	Lt-+Ve	TDT- Ve SISI - 100%	0.10		A	Unchanged
26	vasumathi	0	48	f	66571	Very definite	III	Rt-56dB	Rt-+Ve	TDT- Ve SISI - 100%	0.43		D	Unchanged
27	panneer	0	30	m	12645	Definite	II	Rt-26dB	Rt-+Ve	TDT- Ve SISI - 70%	0.29		B	Unchanged

28	setu	0	30	m	69102	Very definite	III	Rt-50dB	Rt-+Ve	TDT-Ve SISI - 100%	0.60		A	Unchanged
29	mercy	0	22	f	64839	Definite	II	Lt-34dB	Lt-+Ve	TDT-Ve SISI - 80%	0.04		C	Unchanged
30	sethupathi	0	23	m	45781	Very definite	III	Lt-52dB	Lt-+Ve	TDT-Ve SISI - 70%	0.60		B	Unchanged

PATIENT CONSENT FORM

Study Detail: EFFECT OF INTRA TYMPANIC GENTAMICIN THERAPY IN
MENIERE'S DISEASE

Study Centre: Upgraded Institute of Otorhinolaryngology,

Madras Medical Collage & Government General Hospital,
Chennai-3

Patient Name :

Patient Age :

Identification Number :

Patient may tic () these
boxes

I confirm that I have understood the purpose of procedure for the above study. I have the opportunity to ask the question and all my questions and doubts have been answered to my satisfaction.

☐

I understand that my participation in the study is voluntary and that I am free to withdraw at anytime without giving any reason, without my legal rights being effected.

☐

I understand that Investigator, Regulatory authorities and the Ethics committee will not need my permission to look at my health records both in respect to the current study and any further research that may be conducted in relation to it, even if withdraw from the study. I understand that my identity will

☐

not be revealed in any information released to third parties or published, unless as required under the law. I agree not to restrict the use of any data or results that arise from the study.

I was informed about the proceedings of study and any unwanted consequences like hearing loss that can happen in the course of the study. I agree to take part in the above study and to comply with the instructions given and faithfully co-operates with the study team. I agree to inform the study staff immediately if I suffer from any deterioration in my health or well being or any unexpected or unusual symptoms.

I hereby consent to participate in this study.

I hereby give permission to undergo complete clinical examination and diagnostic tests including hematological, biochemical, radiological tests.

Signature/Thumb Impression:

Place:

Date:

Patient Name and Address :

Signature of the Investigator:

Place:

Date:

Study Investigator's Name :

INSTITUTIONAL ETHICAL COMMITTEE
MADRAS MEDICAL COLLEGE, CHENNAI - 3

Telephone No : 044 25305301

Fax : 044 25363970

CERTIFICATE OF APPROVAL

To
Dr. V. Suresh
PG in MS ENT
Madras Medical College, Chennai -3

Dear Dr. V. Suresh

The Institutional Ethical Committee of Madras Medical College reviewed and discussed your application for approval of the project / proposal / clinical trial entitled “ **Effect of intratympanic gentamycin therapy in meniere’s disease**” No 16072010

The following members of Ethical committee were present in the meeting held on 21.07.2010 conducted at Madras Medical College,

- | | |
|---|--------------------|
| 1. Prof. S.K. Rajan, MD | - Chairperson |
| 2. Prof. J. Mohanasundaram, MD,Ph.D,DNB
Dean, Madras Medical College, Chennai -3 | - Deputy Chairman |
| 3. Prof. A. Sundaram, MD
Vice Principal MMC, Chennai -3 | - Member Secretary |
| 4. Prof R. Sathianathan, MD
Director, Institute of Psychiatry | - Member |
| 5. Prof R. Nandhini, MD
Director Institute of Pharmacology, M MC, Ch-3 | - Member |
| 6. Prof Pregna B. Dolia, MD
Director, Institute of Biochemistry, MMC, Ch-3 | - Member |
| 7. Prof. C. Rajendran, MD
Director, Institute of Internal Medicine, MMC, Ch-3 | - Member |
| 8. Prof. Geetha Subramanian, MD,DM
Professor & Head, Dept. Of Cardiology | - Member |
| 9. Prof. V. Shruti Kamal, MS
Professor of Surgery, MMC, Ch-3 | - Member |
| 10. Prof Md. Au, MD, DM
Professor & Head ,Dept. of MGE, MMC, Ch-3 | - Member |

We approve the trail to be conducted in its presented form.

Sd/. Chairman & Other Members

The Institutional Ethics Committee expects to be informed about the progress of the study, any SAE occurring in the course of the study, any changes in the protocol and patient information / informed consent and asks to be provided a copy of the final report

Member Secretary, Ethics Committee.